

Claims:

1. A method for stabilizing dystrophin-associated protein complexes (DAPCs) on the surface of a cell, comprising contacting the cell with an effective amount of biglycan, such that the DAPCs are stabilized.

2. The method of claim 1, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to a portion of biglycan and having at least one biological activity of biglycan.

3. The method of claim 2, wherein the biglycan binds to alpha-dystroglycan.

4. The method of claim 2, wherein the biglycan binds to a alpha-sarcoglycan and/or gamma-sarcoglycan.

5. The method of claim 4, wherein the biglycan further binds to alpha-dystroglycan.

6. The method of claim 2, wherein the biglycan stimulates phosphorylation of alpha-sarcoglycan on a cell membrane.

7. The method of claim 1, wherein the portion of biglycan is one or more 24 amino acids repeat motifs in the Leucine Rich Repeat (LRR) of human biglycan having SEQ ID NO: 9.

8. The method of claim 7, wherein the biglycan comprises an amino acid sequence comprising one or more LRRs of human biglycan having SEQ ID NO: 9.

9. The method of claim 1, wherein the biglycan comprises glycosaminoglycan (GAG) side chains.

10. The method of claim 1, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to amino acids 38-365 of SEQ ID NO: 9.

11. The method of claim 1, wherein the biglycan comprises an amino acid sequence that is at least about 95% identical to amino acids 38-365 of SEQ ID NO: 9.

12. The method of claim 1, wherein the biglycan is encoded by a nucleic acid which hybridizes to SEQ ID NO: 8.

13. The method of claim 1, wherein the biglycan is *Torpedo* DAG-125.

14. The method of claim 1, wherein the cell is a muscle cell.

15. A method for activating a postsynaptic membrane of a cell, comprising contacting the cell with an effective amount of biglycan, such that the postsynaptic membrane is activated.

18. The method of claim 15, wherein the biglycan binds to alpha-dystroglycan.

5 ~~18~~ The method of claim ~~16~~¹⁵, wherein the biglycan potentiates agrin-induced AChR aggregation on the surface of the cell.

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20. The method of claim 15, wherein the biglycan stimulates the phosphorylation of MuSK
on the cell.

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21. The method of claim 15, wherein the biglycan potentiates agrin-induced phosphorylation
10 of MuSK.

~~21~~ 22. The method of claim ~~15~~ 16, wherein the portion of biglycan is one or more 24 amino acids repeat motifs in the Leucine Rich Repeat (LRR) of human biglycan having SEQ ID NO: 9.

23. The method of claim 22, wherein the biglycan comprises an amino acid sequence comprising one or more LLRs of human biglycan having SEQ ID NO: 9.

15 ²³~~24~~. The method of claim ¹⁵~~16~~, wherein the biglycan comprises glycosaminoglycan (GAG) side chains.

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25. The method of claim 16, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to amino acids 38-365 of SEQ ID NO: 9.

25
26. The method of claim 25, wherein the biglycan comprises an amino acid sequence that is
20 at least about 95% identical to amino acids 38-365 of SEQ ID NO: 9.

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27. The method of claim 15, wherein the biglycan is encoded by a nucleic acid which hybridizes to SEQ ID NO: 8.

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28. The method of claim 15, wherein the cell is a muscle cell.

~~28~~
~~30~~. A method for treating or preventing a condition associated with an abnormal dystrophin-associated protein complex (DAPC) in cells of a subject, comprising administering to the subject a pharmaceutically effective amount of biglycan.

~~29~~
~~31.~~ The method of claim ~~30~~²⁸, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to a portion of biglycan and having at least one biological activity of biglycan.

30 ~~32~~³⁰. The method of claim ~~32~~²⁹ wherein the portion of biglycan is one or more 24 amino acids repeat motifs in the Leucine Rich Repeat (LRR) of human biglycan having SEQ ID NO: 9.

~~31~~¹⁵ The method of claim ~~36~~, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to amino acids 38-365 of SEQ ID NO: 9.

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34. The method of claim 15, wherein the biglycan comprises the amino acid sequence having
SEQ ID NO: 9.

5 ³³~~35~~ The method of claim ²⁸~~30~~, comprising administering to the subject a nucleic acid encoding the biglycan.

³⁴
~~36~~ The method of claim ²⁸~~30~~, wherein the condition is characterized by the breakdown of muscle cell membranes.

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~~34~~. The method of claim ~~18~~¹⁷, wherein the condition is a muscular dystrophy selected from the
10 group consisting of Duchenne's Muscular Dystrophy, Becker's Muscular Dystrophy, Congenital
Muscular Dystrophy, Limb-girdle Muscular Dystrophy, and myotonic dystrophy.

~~34~~
~~38~~ A method for treating or preventing a condition characterized by an abnormal neuromuscular junction or synapse in a subject, comprising administering to the subject a pharmaceutically effective amount of biglycan.

15 ~~31~~³¹. The method of claim ~~38~~³⁰, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to a portion of biglycan and having at least one biological activity of biglycan.

~~38~~
~~40~~ The method of claim ~~38~~, wherein the portion of biglycan is one or more 24 amino acids repeat motifs in the Leucine Rich Repeat (LRR) of human biglycan having SEQ ID NO: 9.

20 ~~29~~³⁹. The method of claim ~~36~~³⁶, wherein the biglycan comprises an amino acid sequence which is at least about 90% identical to amino acids 20-365 of SEQ ID NO: 9.

~~42~~⁴⁰ The method of claim ~~38~~³⁶, wherein the biglycan comprises the amino acid sequence having
SEQ ID NO: 9,

~~41~~³⁶ The method of claim ~~38~~³⁶, comprising administering to the subject a nucleic acid encoding
25 the biglycan.

⁴²
~~44~~ The method of claim ²⁰~~38~~, wherein the condition is a neuromuscular or neurological disease.

30 ~~42~~ A method for determining whether a subject has or is at risk of developing a condition associated with an abnormal DAPC or abnormal synapse or neuromuscular junctions, comprising determining the level or activity of biglycan, wherein the presence of an abnormal level and/or activity of biglycan in the tissue of a subject indicates that the subject has or is at risk of

developing a condition associated with an abnormal DAPC or abnormal neuromuscular junctions.

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~~45~~ 43. The method of claim ~~42~~⁴³, wherein the condition is a muscular dystrophy.

~~45~~
~~46~~ 44. The method of claim ~~43~~⁴⁴, wherein the condition is selected from the group consisting of
5 Duchenne's Muscular Dystrophy, Becker's Muscular Dystrophy, Congenital Muscular Dystrophy, Limb-girdle Muscular Dystrophy, and myotonic dystrophy.

~~46~~
~~47~~ 45. A composition comprising a pharmaceutically efficient amount of biglycan or a portion thereof that is sufficient for stabilizing DAPCs or activating postsynaptic membranes.

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~~48~~ 46. A method for identifying an agent which modulates the interaction between α -dystroglycan and biglycan, comprising contacting an α -dystroglycan peptide with biglycan or a
10 portion thereof sufficient for binding to α -dystroglycan and a test compound in conditions under which the α -dystroglycan peptide and biglycan interact in the absence of the test compound, wherein a difference in the level of binding between the α -dystroglycan peptide and biglycan in the presence of the test compound relative to the absence of the test compound indicates that the
15 test compound is an agent which modulates the interaction between α -dystroglycan and biglycan.

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~~49~~ 47. A method for identifying an agent which modulates the interaction between α -sarcoglycan and biglycan, comprising contacting an α -sarcoglycan peptide with biglycan or a
20 portion thereof sufficient for binding to α -sarcoglycan peptide and a test compound in conditions under which the α -sarcoglycan peptide and biglycan interact in the absence of the test compound, wherein a difference in the level of binding between the α -sarcoglycan peptide and biglycan in the presence of the test compound relative to the absence of the test compound indicates that the test compound is an agent which modulates the interaction between α -sarcoglycan and biglycan.

~~49~~
~~50~~ 48. A method for identifying an agent which modulates the interaction between α -dystroglycan and a sarcoglycan component, comprising contacting an α -dystroglycan peptide
25 with the sarcoglycan component or a portion thereof sufficient for binding to α -dystroglycan and a test compound in conditions under which the α -dystroglycan peptide and the sarcoglycan component interact in the absence of the test compound, wherein a difference in the level of binding between the α -dystroglycan peptide and the sarcoglycan component in the presence of the test compound relative to the absence of the test compound indicates that the test compound
30 is an agent which modulates the interaction between α -dystroglycan and the sarcoglycan component.

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~~51~~ 49. A method for identifying an agent which modulates the interaction between MuSK and biglycan, comprising contacting biglycan with MuSK or a portion thereof sufficient for binding

to biglycan and a test compound in conditions under which biglycan and MuSK interact in the absence of the test compound, wherein a difference in the level of binding between the biglycan and MuSK in the presence of the test compound relative to the absence of the test compound indicates that the test compound is an agent which modulates the interaction between biglycan and MuSK.

51 ✓ A method for identifying a compound which modulates the phosphorylation of alpha-sarcoglycan or MuSK in a cell, comprising contacting a cell comprising alpha-sarcoglycan or MuSK with a compound and determining the level of phosphorylation of alpha-sarcoglycan or MuSK, respectively, wherein an difference in the level of phosphorylation of alpha-sarcoglycan or MuSK in the presence relative to the absence of the compound indicates that the compound modulates the phosphorylation of alpha-sarcoglycan or MuSK.

51 ✓ A method for identifying a compound which modulates the phosphorylation of alpha-sarcoglycan or MuSK by biglycan in a cell, comprising contacting a cell comprising alpha-sarcoglycan or MuSK with biglycan and a compound, and determining the level of phosphorylation of alpha-sarcoglycan or MuSK, respectively, wherein an difference in the level of phosphorylation of alpha-sarcoglycan or MuSK in the presence relative to the absence of the compound indicates that the compound modulates the phosphorylation of alpha-sarcoglycan or MuSK by biglycan.